REMARKS

This responds to the Office Action mailed on August 26, 2005, and the references cited therewith.

Claims 1-68 are now pending in this application. However, the Examiner has withdrawn claims 1-40, 43-47, 49-53 and 56-68 from examination in view of the Restriction Requirement dated March 10, 2005. Therefore, claims 41, 42, 48, 54 and 55 are now under examination.

The term "binding entity" in claims 41, 42, 48, 4 and 55 has been replaced with "antibody," and the dependencies of claims 54 and 55 has been changed from claim 40 (withdrawn) to claim 41 (under examination). Support for subject matter relating to antibodies can be found throughout the specification and claims, for example, at page 41, line 9 to page 53, line 17 and in the Examples. In addition, Terminology relating to "more efficiently" in claim 42 and "less efficiently" in claim 54 has been deleted and replaced with terminology relating to "substantially no binding." Terminology relating to "more efficiently" in claim 42 and "less efficiently" in claim 54 has been deleted and replaced with terminology relating to "substantially no binding." Support for subject matter relating to antibodies that exhibit substantially no binding to non-phosphorylated or phosphorylated peptides can be found throughout the specification and claims, for example, at page 41, lines 11-16 and in the Examples. Applicant submits that no new matter has been added to the specification.

Personal Interview

Applicant wishes to thank the Examiner for extending the courtesy of a personal interview to Applicant's representative, Robin A. Chadwick, on May 17, 2005.

The Restriction Requirement dated March 10, 2005 was discussed. The Examiner confirmed that the unelected species would be examined if the elected species was found to be patentable in view of the prior art.

This account is believed to be a complete and accurate summary of the interview as required by 37 C.F.R. § 1.133. If the Examiner believes that this summary is inaccurate or incomplete, Applicants respectfully request that the Examiner point out any deficiencies in his next communication so that Applicants can amend or supplement the interview summary.

Restriction Requirement

The Examiner has withdrawn claims 1-40, 43-47, 49-53 and 56-68 from examination in view of the Restriction Requirement dated March 10, 2005.

Objection to the Specification

At page 4 of the Office Action, the Examiner objects to the disclosure alleging that there are no SEQ ID Nos. for the sequences presented in Figure 20. In the Brief Description of the Figures of the instant application, specifically on page 9, lines 21-23, Applicant provides a description of Figure 20. The description of Figure 20 concludes with the phrase "(SEQ ID NOs:632-640)." SEQ ID NOs: 632-640 represent the sequences listed in Figure 20, which are also listed in the Sequence Listing under the numbers 632-640. MPEP § 2422.02 states that "the sequence identifier ('SEQ ID NO:X') must be used, either in the drawing or in the Brief Description of the Drawings." Since the sequence identifiers for Figure 20 are provided in the Brief Description of the Figures of the instant application, Applicant respectfully submits that the specification is in compliance with the sequence listing requirements of 37 C.F.R. §§ 1.821-1.825. Thus, Applicant respectfully requests withdrawal of the objection to the disclosure.

§112, First Paragraph, Rejection of the Claims

Claims 41, 42, 48, 54 and 55 were rejected under 35 U.S.C. § 112, first paragraph, as allegedly lacking written description. The Examiner alleges that the specification does not adequately describe binding entities other than antibodies. The claims are presently drawn to antibodies. Withdrawal of this rejection is respectfully requested.

§112, Second Paragraph, Rejection of the Claims

Claims 42 and 54 were rejected under 35 U.S.C. § 112, second paragraph, as allegedly indefinite. According to the Examiner, the term "more efficiently" in claim 42 and "less efficiently" in claim 54 is indefinite. Terminology relating to "more efficiently" in claim 42 and "less efficiently" in claim 54 has been deleted and replaced with terminology relating to "substantially no binding." Withdrawal of this rejection is respectfully requested.

§103 Rejection of the Claims

Claims 41, 42, 48, 54 and 55 were rejected under 35 U.S.C. § 103(a) as allegedly unpatentable over Polakiewicz et al. (U.S. Application publication No. 2004/00977130) in view of Freeman (U.S. Patent 5536636) and Laudano et al. (U.S. Patent 6,924,361). According to the Examiner, Polakiewicz et al. discloses antibodies that selectively bind to phosphorylated IRS-1 and IRS-2, where the IRS-1 and/or IRS-2 are phosphorylated at Ser1101 and/or Ser1149, respectively. The Examiner admits that Polakiewicz et al. does not disclose any of the presently claimed sequences, but asserts that Freeman discloses a polypeptide that includes peptidyl sequence SEQ ID NO:320, citing to FIG. 2 of Freeman (residues 584-595). The Examiner further asserts that the polypeptide disclosed by Freeman is a tyrosine phosphatase with SH2 domains, and that Laudano generally discloses phosphopeptide-specific antibodies.

Claim 41 is directed to an antibody whose binding differentiates between a defined phosphorylated peptide having any one of SEQ ID NO:298-347, 349-473 and a non-phosphorylated peptide that differs from the defined peptide by substitution of Ser for the pSer or substitution of a Thr for the pThr, and wherein the antibody has substantially no binding to a phosphorylated peptide having SEQ ID NO: 229 (WKN-pS-IRH).

This rejection is respectfully traversed. To establish a *prima facie* case of obviousness, three basic criteria must be met. First, there must be some suggestion or motivation either in the cited references themselves or in the knowledge generally available to an art worker, to modify the reference or to combine reference teachings so as to arrive at the claimed combination. Second, the art must provide a reasonable expectation of success. Finally, the prior art references must teach or suggest all the claim elements (MPEP § 2143). The teaching or suggestion to arrive at the claimed combination and the reasonable expectation of success must both be found in the prior art, not in Applicant's disclosure (MPEP § 2143, citing with favor *In re Vaeck*, 20 USPQ2d 1438 (Fed. Cir. 1991)).

Applicant first submits that the combination of references do not teach or suggest all the claim elements. In particular, the combination of Polakiewicz et al., Freeman et al, and Laudano et al. do not disclose or teach peptide SEQ ID NO:298-347, 349-473. Hence, there is no

disclosure or teaching in this combination of references that antibodies can bind specifically to these peptides when they are phosphorylated.

Thus, Polakiewicz et al. is limited to disclosure and teachings on insulin receptor substrate-1 and -2, and provides no disclosure or teaching of peptides with SEQ ID NO:298-347, 349-473, or that these peptides can be phosphorylated, or that an antibody can bind to any of these phosphopeptides. At best, Polakiewicz et al. teach antibodies with some specificity to phosphorylated insulin receptor substrate-1 and/or -2.

Freeman et al. is limited to disclosure of methods for isolating genes that encode tyrosine phosphatases. While providing a sequence for SH-PTP1 and SH-PTP2, Freeman et al. do not disclose or recognize specific sites of phosphorylation within SH-PTP1 and SH-PTP2. Nor do Freeman et al. disclose antibodies that can recognize phosphorylated SH-PTP1 and SH-PTP2 where those antibodies do not recognize the non-phosphorylated SH-PTP1 and SH-PTP2 polypeptides.

Laudano et al. discloses nothing whatsoever about SHP, or anything about peptide SEQ ID NO:298-347, 349-473. Instead, Laudano et al. are limited to a generalized disclosure of methods for isolating antibodies that recognize phosphopeptides, where the methods provided by Laudano et al. involve removing contaminating antibodies that do not recognize phosphopeptides.

Hence, at least one critical and non-obvious element is missing from the combination of references cited by the Examiner -- the epitopes (SEQ ID NO:298-347, 349-473) recognized and claimed by Applicants.

Second, there is no suggestion or motivation in the cited references (or in the knowledge generally available to an art worker), to modify the reference or to combine reference teachings so as to arrive at the claimed invention. The elements missing from the cited references include the exact sequences of the phosphorylated or non-phosphorylated peptides to which the antibodies bind.

Simple recognition that *some* tyrosine and *some* serine residues are phosphorylated is not recognition that a *specific* serine or tyrosine in a specific peptidyl sequences is the actual target for phosphorylation *in vivo*, while other tyrosine and serine residues are not. For example, there are about 59 Ser and Tyr residues in the sequence provided by Freeman in FIG. 2. One of skill

in the art would have no way to select which of these 59 residues might be phosphorylated and which would not be phosphorylated based on the teachings of the combined references. Nothing in the references cited by the Examiner would permit the skilled artisan to derive the sequences of SEQ ID NO:298-347, 349-473 or motivate that artisan to make antibodies against any one of those peptides. Therefore, the combination of references would not suggest the invention or motivate the skilled artisan to arrive at the claimed invention. The combination of references simply does not provide enough information, nor a suggestion that the little information provided on unrelated insulin receptor substrate and SH-PTP proteins should even be combined.

Third, the skilled artisan could not reasonably hope to successfully derive the phosphorylated sequences of SEQ ID NO:298-347, 349-473 given the teachings of Polakiewicz et al., Freeman et al, and Laudano et al. because none of these references disclose these sequences as being phosphorylated or otherwise as potentially useful. Three problems would face the skilled artisan in attempting to derive the invention from the Polakiewicz et al., Freeman et al, and Laudano et al. references. First, the skilled artisan would have no knowledge permitting him or her to select any of the SEQ ID NO:298-347, 349-473 sequences, and not some other sequence(s). Second, the skilled artisan would not know that these sequences (and not other sequences) are actually phosphorylated, and therefore would have no recognition of their utility. Third, the skilled artisan would not know that he or she could or should make antibodies to those peptidyl sequences (and not to some other sequences). Accordingly, one of skill in the art could not reasonably harbor an expectation of successfully deriving the invention from the teachings of the cited references.

Therefore, the subject matter of claim 41 is novel and non-obvious in view of the Polakiewicz et al., Freeman et al, and Laudano et al. references. Claims 42, 48, 54 and 55 depend from and therefore include all elements of claim 41. Hence, claims 42, 48, 54 and 55 are also novel and non-obvious.

Withdrawal of this rejection is respectfully requested.

CONCLUSION

Applicant respectfully submits that the claims are in condition for allowance, and notification to that effect is earnestly requested. The Examiner is invited to telephone Applicant's attorney at (516) 795-6820 to facilitate prosecution of this application.

If necessary, please charge any additional fees or credit overpayment to Deposit Account No. 19-0743.

Respectfully submitted,

JAMES STEPHEN SHAW

By his Representatives,

SCHWEGMAN, LUNDBERG, WOESSNER & KLUTH, P.A.
P.O. Box 2938
Minneapolis, MN 55402
(516) 795-6820

Date November 22, 2005

By _____
Robin A. Chadwick
Reg. No. 36,477

CERTIFICATE UNDER 37 CFR 1.8: The undersigned hereby certifies that this correspondence is being deposited with the United States Postal Service with sufficient postage as first class mail, in an envelope addressed to: ~~Mail Stop~~ Amendment, Commissioner of Patents, P.O. Box 1450, Alexandria, VA 22313-1450, on this 22nd day of November, 2005.

Patricia A. Hultman
Name

Signature